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Customer No. 22,852

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(I)

--17. A group A streptogramin derivative of formula (I) or a salt thereof:

wherein:

- R₁ is chosen from -NR'R" groups, wherein
 - R' is chosen from a hydrogen atom and a methyl group, and
 - R" is chosen from
 - a hydrogen atom, (i)
 - alkyl groups, (ii)
 - cycloalkyl groups, (iii)
 - an allyl group, (iv)
 - a propynyl group, (v)
 - a benzyl group, (vi)
 - -OR" groups, wherein R" is chosen from a hydrogen atom, alkyl (vii) groups, cycloalkyl groups, an ally group, a propynyl group, and a benzyl group, and

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(viii) -NR₃R₄ groups wherein

- R₃∖and R₄ are each a methyl group, or
- R₃ and R₄, which are identical or different, form, together with the nitrogen atom to which they are attached, a saturated or unsaturated 4- to 5-membered heterocyclyl group, wherein one of said members, in addition to said nitrogen atom, may be an atom chosen from an oxygen atom, a sulphur atom, and a nitrogen atom,
- R₂ is chosen from a hydrogen atom, a methyl group, and an ethyl group,
- the bond ____ is a single bond or a double bond,
- unless otherwise stated, said alkyl groups are chosen from straight and branched $C_1\text{-}C_6$ alkyl groups,
- unless otherwise stated, said cycloalkyl groups are chosen from C₃-C₄ cycloalkyl groups,
- when R" is chosen from a group other than said -OR" groups and said -NR₃R₄ groups, said group A streptogramin derivative is chosen from R-epimers and mixtures of R- and S-epimers, wherein said R-epimer is predominant, and

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FINNEGAN, HENDERSON,
FARABOW, GARRETT,
8 DUNNER, L. L. P.
1300 I STREET, N. W.
WASHINGTON, DC 20005

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- when R" is chosen from said -OR" groups and said -NR₃R₄ groups, said group A streptogramin derivative is chosen from R-epimers, S-epimers, and mixtures of R- and S-epimers.

- 18. A group A streptogramin derivative according to claim 17, wherein:
- R₁ is chosen from -NR'R' groups, wherein
 - R' is chosen from a hydrogen atom and a methyl group, and
 - R" is chosen from
 - (i) a hydrogen atom,
 - (ii) alkyl groups,
 - (iii) cycloalkyl groups,
 - (iv) an allyl group,
 - (v) a propynyl group,
 - (vi) a benzyl group,
 - (vii) -OR''' groups, wherein R''' is chosen from C_1 - C_6 alkyl groups, an allyl group, and a propynyl group,
 - (viii) -NR₃R₄ groups, wherein
 - R₃ and R₄ are each a methyl group, or
 - R₃ and R₄, which are identical or different, form, together with the nitrogen atom to which they are attached, a saturated or unsaturated 4- to 5-membered peterocyclyl group, wherein one



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of said members, in addition to said nitrogen atom, may be an atom chosen from an oxygen atom, a sulphur atom, and a PECEIVED nitrogen atom, MAY 3 1 2001

- R₂ is chosen from a hydrogen atom, a methyl group, and an ethyl group,

- the bond ____ is a single bond or a double bond,

- when R" is chosen from a group other than said -OR" groups and said -NR $_3$ R $_4$ groups, said group A streptogramin derivative is chosen from R-epimers and mixtures of R- and S-epimer's, wherein said R-epimer is predominant, and

- when R" is chosen from said -OR" groups and said -NR₃R₄ groups, said group A streptogramin derivative is chosen from R-epimers, S-epimers, and mixtures of R- and S-epimers.

- A group A streptogramin derivative according to claim 17, wherein: 19.
- R₁ is chosen from -NR'R" groups, wherein
 - R' is chosen from a hydrogen atom and a methyl group, and
 - R" is chosen from
 - a hydrogen atom, (i)
 - C₁-C₄ alkyl groups, (ii)

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- (iii) cydloalkyl groups,
- (iv) an allyl group,
- (v) a propynyl group,
- (vi) a benzy\group,
- (vii) -OR" groups, wherein R" is chosen from C_1 - C_3 alkyl groups, an allyl group, and a propynyl group,
- (viii) -NR₃R₄ groups, wherein
 - R₃ and R₄, which are identical or different, form, together with the nitrogen atom to which they are attached, a 5-membered saturated heterocyclyl group,
- R₂ is chosen from a methyl group and an ethyl group,
- the bond ---- is a single bond or a double bond,
- when R" is chosen from a group other than said -OR" groups and said -NR₃R₄ groups, said group A streptogramin derivative is chosen from R-epimers and mixtures of R- and S-epimers, wherein said R-epimer is predominant, and
- when R" is chosen from said -OR" groups and said -NR₃R₄ groups, said group A streptogramin derivative is chosen from R-epimers, S-epimers, and mixtures of R- and S-epimers.

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20. A group A streptogramin derivative according to claim 17, wherein said group A streptogramin is (16R)-16-dimethylamino-16-deoxopristinamycin II_A or a salt thereof.

21. A group A streptogramin derivative according to claim 17, wherein said group A streptogramin is (16R)-16-methoxyamine-16-deoxopristinamycin II_B or a salt thereof.

22. A group A streptogramin derivative according to claim 17, wherein said group A streptogramin is (16R)-16-ethoxyamino-16-deoxopristinamycin II_B or a salt thereof.

23. A group A streptogramin derivative according to claim 17, wherein said group A streptogramin is (16R)-16-allyloxyamino-16-deoxopristinamycin II_B or a salt thereof.

24. A group A streptogramin derivative according to claim 17, wherein said group A streptogramin is (16R)-16-methoxyamino-16-deoxopristinamycin II_A or a salt thereof.

25. A process for preparing a group A streptogramin derivative according to claim 17, said process comprising:

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARNETT,
8 DUNNER, ALP
1300 I STREET N.W.
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(a) preparing a group A streptogramin derivative, wherein R' is a hydrogen atom, by reacting, in the presence of a reducing agent, an amine of formula (III):

H₂N-R" (III)

wherein R" is defined as in claim 17 with a natural pristinamycin of formula (II):

$$H_3C/I_{M_1}$$

$$H_3C$$

$$R_2$$

$$Wherein R_2 is defined as in claim 17,$$

(b) optionally reacting said group A streptogramin derivative of formula (I), wherein R' is a hydrogen atom, with formaldehyde or a formaldehyde derivative capable of generating formaldehyde in situ to form a second intermediate compound, and then reacting said second intermediate compound with a reducing agent to form a group A streptogramin derivative, wherein R' is a methyl group, and

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- (c) optionally converting said group A streptogramin derivative of formula (I), prepared by (a) or (b) above, to a salt and/or separating its R-epimer.
- 26. A process for preparing a group A streptogramin derivative according to claim 17, said process comprising:
- (a) preparing an intermediate compound of formula (IV):

wherein $\rm R_2$ and $\rm R^{"}$ are defined as in claim 17 by reacting an amine of formula (III):

H₂N-R" (III)

wherein R" is chosen from -OR" groups, and wherein said R" groups are defined as in claim 17

with a natural pristinar nycin of formula (II):

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$$H_3C$$
 M_3C
 M_3C

wherein R_2 is defined as in claim 1/7,

(b) isolating said intermediate compound of formula (IV),

reacting said isolated intermediate compound of formula (IV) with a reducing agent to prepare a group A streptogramin derivative of formula (I), wherein R' is a hydrogen atom,

(d) optionally reacting said group A streptogramin derivative of formula (I), wherein R' is a hydrogen atom, with formaldehyde or a formaldehyde derivative capable of generating formaldehyde in situ to form a second intermediate compound, and then reacting said second intermediate compound with a reducing agent to form a group A streptogramin derivative of formula (I), wherein R' is a methyl group, and

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- (e) optionally converting said group A streptogramin derivative of formula (I), prepared by (c) or (d) above, to a salt and/or separating its R-epimer.
- 27. A process for preparing a group A streptogramin derivative according to claim 17, said process comprising:
- (a) preparing a group A streptogramin derivative, wherein R' is a hydrogen atom,by reacting, in the presence of a reducing agent:
 - (1) a ketone, chosen according to a desired R" group, wherein said R" is as defined in claim 17, with
 - (2) an amine-containing derivative of formula (V):

wherein R₂ is as defined in claim 17,

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- (b) optionally reacting said group A streptogramin derivative of formula (I), wherein R' is a hydrogen atom, with formaldehyde or a formaldehyde derivative capable of generating formaldehyde in situ to form a second intermediate compound, and then reacting said second intermediate compound with a reducing agent to form a group A streptogramin derivative, wherein R' is a methyl group, and
- (c) optionally converting said group A streptogramin derivative of formula (I), prepared by (a) or (b) above, to a salt and/or separating its R-epimer.
- 28. A composition comprising at least one group A streptogramin derivative of formula (I) or salt thereof according to claim 17 and at least one group B streptogramin derivative.
- 29. A composition according to claim 28, wherein said at least one group B streptogramin derivative is chosen from natural group B streptogramin components and semisynthetic group B streptogramin components.
- 30. A composition according to claim 28, wherein said at least one group B streptogramin derivative is chosen from pristinamycin I_A , pristinamycin I_B , pristinamycin I_C , pristinamycin I_C

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FARABOW, GARRETT,
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virginiamycin S_1 , virginiamycin S_3 , virginiamycin S_4 , vernamycin S_4 , ve

31. A composition according to claim 28, wherein said at least one group B streptogramin derivative is chosen from semisynthetic group B streptogramin derivatives of formula (A):

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wherein:

- (1) Rb, Rc, Re, and Rf are each a hydrogen atom;
 - Rd is chosen from a hydrogen atom and a dimethylamino group; and
 - Ra is chosen from:

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- (A) -CH₂R'a groups, wherein R'a is chosen from:
 - (i) a 3-pyrrolidinylthio group,
 - (ii) a 3-piperidylthio group,
 - (iii) a 4-piperidylthio group,
 - wherein said groups (i)-(iii) may be unsubstituted or substituted with at least one group chosen from alkyl groups, and
 - (iv) alkylthio groups which are substituted with 1 or 2 groups chosen from:
 - (a) a hydroxysulfonyl group,
 - (b) alkylamino groups,
 - (c) dialkylamino groups, which may be unsubstituted or substituted with at least one group chosen from a mercapto group or dialkylamino groups,
 - (d) a piperazine ring, a morpholino group, a thiomorpholino group, a piperidino group, a 1-pyrrolidinyl group, a 2-piperidyl group, and a 4-piperidyl group, a 2-pyrrolidinyl group, and a 3-pyrrolidinyl group, each of which may be unsubstituted or substituted with alkyl, and
 - (B) =CHR'a groups, wherein R'a is chosen from:
 - (i) a 3-pyrrolidinylamino group,
 - (ii) a 3-piperidylamino group and a 4-piperidylamino group,

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FINNECAN, HENDERSON, FARABOW, GARRETT, 8 DUNNER, L. L. P.

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- (iii) a 3-pyrrolidinyloxy group,
- (iv) a 3-piperidyloxy group and a 4-piperidyloxy group,
- (v) a 3-pyrrolidinylthio group,
- (vi) a 3-piperidylthio group and a 4-piperidylthio group,
- wherein said groups (i)-(vi) may be unsubstituted or substituted
 with at least one group chosen from alkyl groups,
- (vii) alkylamino groups,
- (viii) alkyloxy groups, and
- (ix) alkylthio groups which are substituted with 1 or 2 groups chosen from:
 - (a) a hydroxysulfonyl group,
 - (b) alkylamino groups,
 - (c) dialkylamino groups unsubstituted or substituted with at least one group chosen from dialkylamino groups,
 - (d) trialkylammonio groups,
 - (e) a 4-imidazolyl group, and a 5-imidazolyl group, each of which may be unsubstituted or substituted with alkyl,
 - (f) a piperazine ring, a morpholino group, a thiomorpholino group, a piperidino group, a 1-pyrrolidinyl group, a 2-piperidyl group, a 3-piperidyl group, a 4-piperidyl group, a 2-pyrrolidinyl group, and a 3-pyrrolidinyl group, each of which may be unsubstituted or substituted with alkyl,



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- (C) a 3-quinuclidinylthiomethyl group, and
- (D) a 4-quinuclidinylthiomethyl group; or
- (2) Ra is a hydrogen atom, and
 - (a) Rb, Re, and Rf are each a hydrogen atom, and
 - Rd is chosen from a -NHCH₃ group and a -N(CH₃)₂ group, and Rc is chosen from a chlorine atom and a bromine atom, or when Rd is a -N(CH₃)₂ group, Rc is chosen from (C₃-C₅) alkenyl groups, or
 - (b) Rb, Rd, Re, and Rf are each a hydrogen atom, and
 - Rc is chosen from halogen atoms, aminomonoalkyl groups,
 aminodialkyl groups, alkyloxy groups, a trifluoromethyloxy group,
 thioalkyl groups, (C₁-C₃) alkyl groups, and trihalomethyl groups, or
 - (c) Rb, Rc, Re, and Rf are each a hydrogen atom, and
 - Rd is chosen from halogen atoms, an ethylamino group, a diethylamino group, a methylethylamino group, alkyloxy groups, a trifluoromethyloxy group, thioalkyl groups, (C₁-C₆) alkyl groups, aryl groups, and trihalomethyl groups, or
 - (d) Rb, Re, and Rf are each a hydrogen atom,
 - Rc is chosen from halogen atoms, aminomonoalkyl groups,
 aminodialkyl groups, alkyloxy groups, a trifluoromethyloxy group,
 thioalkyl groups, and (C₁-C₃) alkyl groups, and

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- Rd is chosen from halogen atoms, an amino group, aminomonoalkyl groups, aminodialkyl groups, alkyloxy groups, a trifluoromethyloxy group, thioalkyl groups, (C₁-C₆) alkyl groups, and trihalomethyl groups, or
- (e) Rc, Re, and Rf are each a hydrogen atom, and
 - Rb and Rd are each a methyl group.
- 32. A pharmaceutical composition comprising at least one group A streptogramin derivative of formula (I) or salt thereof according to claim 17, wherein said composition optionally comprises at least one agent chosen from pharmaceutically acceptable diluents and pharmaceutically acceptable adjuvants.
- 33. A pharmaceutical composition comprising at least one group A streptogramin derivative of formula (1) or salt thereof according to claim 17 and at least one group B streptogramin derivative, wherein said composition optionally comprises at least one agent chosen from pharmaceutically acceptable diluents and pharmaceutically acceptable adjuvants. --